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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/120,970	07/22/1998	ROY CURTISS III	53116-1763	2800

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EXAMINER

PORTNER, VIRGINIA ALLEN

ART UNIT PAPER NUMBER

1645

DATE MAILED: 11/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/120,970

Applicant(s)

CURTISS ET AL.

Examiner

Ginny Portner

Art Unit

1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 10 June 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 30,32-39,41-51 and 53-65 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 30,32-39,41-51 and 53-65 is/are rejected.
- 7) ☒ Claim(s) 35 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

Claims 30,32-33,35-39,41-51,53-65 are pending.

#### **Objections/Rejections Withdrawn**

1. (Claim Objections Withdrawn) Claims 35, 52 and 65 objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim has been obviated through amendment or cancellation of claims.
2. Claims 43,44-45,47,51,53-55 and 60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reciting abbreviations that do not clearly define the claimed invention as the meaning of the abbreviations is not structurally, nor functionally defined in the claims, in light of the amendment of the claims and remarks clarifying the terms of the claims.
3. Claim 30, 32-33,35-38, 39, 50-60 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over US Pat.5,294,441; 5,387,744; 5,855,879 and 5,855,880 are herein withdrawn in light of Applicant's remarks and the recombinant bacteria requiring the essential gene that is not chromosomally associated to be under the control of an environmentally regulate-able control sequence.
4. (35 U.S.C. 112, second paragraph, Rejection Withdrawn) Claims 30 and 65 rejected under, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention have been obviated in light of the claim amendments to provide for antecedent basis for the term chromosomal copy and amendment of claim 65 to depend from claim 30.

#### **Objections/Rejections Maintained**

5. (Claim Objection Maintained) Claims 35 objected to for minor informalities, specifically claim 35 is still objected to for depending from a later number claim 39, in light of the fact that claim 35 still depends from claim 39.
6. (Claim Rejections - 35 USC § 112 Maintained) The rejection of Claims 61-64 under 35 U.S.C. § 112, first paragraph as failing to provide an enabling disclosure in light of the fact that the extra chromosomal vector comprising pMEG-104 is required to practice the claimed invention and not so described, known and readily available to the public or obtainable by a repeatable method set forth in the specification was not addressed and therefore maintained for reasons of record.
7. Claim 30, 32-33,35-38, 39-60, 65 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over US Pat 6,780,405 is maintained for reasons of record and responses set forth below to Applicant's remarks.

*Response to Arguments*

8. Applicant's arguments filed June 10, 2005 have been fully considered but they are not persuasive.

9. Applicant asserts that:

a. "The object of the '405 patent is to design a system that produces and releases large amounts of antigen at a desired time, e.g. after inoculation. It is not seen how this RAV system can be considered an obvious variant of an ELV system designed for biological containment, ie, to prevent the vaccine microorganism from surviving in selected non-permissive environments.

10. It is the position of the examiner that the claimed microorganisms of '405 are utilized in the allowed method of inducing immunoprotection in a vertebrate (allowed claim 24), the method comprising the step of "administering the vaccine ".

11. The compositions of '405 are defined by the allowed claims and the definitions provided by the Specification disclosure of '405. Claim 7 of '405 is directed to a microorganism which comprises an environmentally regulatable control sequence, specifically araCPbad, which is activate able by arabinose AraCPbad regulatable control sequence is disclosed to function as a trans regulatory element. A portion of the '405 Specification is quoted immediately below to show one of the definitions of the AraCPbad regulatory control sequence:

- "Depending on the turnover of the trans regulatory element and the relationship between the amount of trans regulatory element on hand and the amount of trans regulatory element needed to maintain the low copy number regime, the low copy number regime can be maintained for several generations after transfer to the high copy number environment. Such temporary low copy

number condition can be useful, for example, for allowing the host microorganism to colonize the host in a high copy number environment (e.g., without arabinose), such as an animal, but not remain indefinitely. As such, the RADS is a **containment system** even without the phage lysis genes described in WO96/40947. A delayed RADS is also useful when the desired gene product is harmful to the host cell, as in Example 3. Additionally, the delayed RADS can be used to depend an essential gene of a balanced lethal host system, such as *asd*, on an activateable control sequence such as araCP.sub.BAD, to provide for a weakening of the cell wall upon immunization (and withdrawal of, in this case, arabinose). See Example 5.”

Additionally, the Specification of ‘405 defines the RAV and RAD system to also comprise an ELV system; this preferred embodiment comprising the araCPbad environmentally regulatable control sequence. Quoting the Specification :

- “A preferred method for causing this lysis is an ELVS system, as described in WO96/40947. In that system, vector-borne lethal genes such as the phage lysis genes *lys 13* and *lys 19* are operably linked to P22 P.sub.R and the chromosome-encoded C2 repressor is operably linked to araCP.sub.BAD. Introduction of the strain into an environment without arabinose, such as in an inoculated animal, results in a dilution of the C2 repressor present until the lethal gene products kill the cell. In addition, the RADS with a RAV comprising a transfer vector can be designed as an ELVS that lysis due to regulated lysis genes inserted into the chromosome. Such expression of lysis genes would exhibit delayed expression such that lysis would only occur after the vertebrate cells with the transfer vector had entered a eukaryotic cell and conferred runaway vector replication. See also Example 6, which describes novel transfer vector adaptations to the RADS.

When properly designed, the ELVS system is fully compatible with the RADS system and may share control elements. In this case, lysis of the cell, for example caused by an ELVS, will release the transfer vector inside the recipient cell. For expression of genes on the transfer vector in recipient cells, it is preferred that the expression genes be operatively linked to expression control sequences operable in the recipient cell. For example, where the recipient cell is an animal cell, it is preferred that the expression genes be operatively linked to a promoter functional in the animal and possess sequences ensuring polyadenylation of the mRNA. Methods for engineering such sequences are well known in the art.” (emphasis added)

- The microorganism of allowed claim 7 of ‘405 is defined to comprise not only the RAD/RAV system, but also to comprise the ELVS system and is administered in the method of allowed claim 24. Therefore, the allowed claim 24 of ‘405 is directed to a species which utilizes a specific environmentally regulatable control sequence, specifically araCPbad. The allowed species anticipates the instantly claimed genus of method now claimed. Additional claims were added to the ODP rejection in light of the amendment of claim 65 to depend from claim 65, and the specific definitions of the allowed species of regulatable control sequence provided by ‘405 to be in trans relationship to an essential *asd* gene, and lysis genes from bacteriophage P22. The obviousness type double patenting rejection is herein maintained.

### ***Conclusion***

1. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. See references cited below.

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US-6,610,529 B1	08-2003	Curtiss et al.	
US-2003/0157071 A1	08-2003	Wolfe et al.	
US-2003/0082511	05-2003	Brown et al.	
US-5,294,441 A	03-1994	Curtiss, III, Roy	
US-5,656,488	08-1997	Curtiss et al.	
US-5,672,345	09-1997	Curtiss, III, Roy	
1516458	09-1976	Gb	
Curtiss III, R, Release of Genetically engineered microorganisms, Chapter 2, pages 7-20, 1988.			
Curtiss III, Roy, Genetic Manipulation of microorganisms: Potential benefits and biohazards, pages 507-533, Ann.			

2. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

3. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
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